SEQUENCE LISTING

<110> BERDEL, Wolfgang E. MESTERS, Rolf M.										
<120> Fusion polypeptides for antivascular tumor therapy										
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<150> PCT/EP04/009364 <151> 2004-08-20										
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Val Tyr Thr Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys 35 40 45										
Cys Phe Tyr Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val 50 55 60										
Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala 70 75 80										
Gly Asn Val Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn 85 90 95										
Ser Pro Glu Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr										
Ile Gln Ser Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu 115 120 125										

Asp Glu Arg Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg 130 135 140

Asp Val Phe Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser 145 150 155 160

Ser Ser Ser Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu 165 170 175

Ile Asp Val Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val 180 185 190

Ile Pro Ser Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu
195 200 205

Cys Met Gly Gln Glu Lys Gly Glu Phe Arg Glu Ile Phe Tyr Ile Ile 210 215 220

Gly Ala Val Val Phe Val Val Ile Ile Leu Val Ile Ile Leu Ala Ile 225 230 235 240

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Thr Asn Phe Lys Thr Ile Leu Glu Trp Glu Pro Lys Pro Val Asn Gln
20 25 30

Val Tyr Thr Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys 35 40 45

Cys Phe Tyr Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val 50 55 60

Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala 65 70 75 80

- Gly Asn Val Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn 85 90 95 Ser Pro Glu Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr

Ile Gln Ser Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu 115 120 125

Asp Glu Arg Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg 130 135 140

Asp Val Phe Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser 145 150 155 160

Ser Ser Ser Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu 165 170 175

Ile Asp Val Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val 180 185 190

Ile Pro Ser Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu
195 200 205

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Val Tyr Thr Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys 35 40 45

Cys Phe Tyr Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val 50 55 60

Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala 65 70 75 80

Gly Asn Val Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn 85 90 95

Ser Pro Glu Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr 100 105 110

- Ile Gl
n Ser Phe Glu Gl
n Val Gly Thr Lys Val As
n Val Thr Val Glu
 115 120 125
- Asp Glu Arg Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg 130 135 140
- Asp Val Phe Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser 145 150 155 160
- Ser Ser Ser Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu 165 170 175
- Ile Asp Val Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val 180 185 190
- Ile Pro Ser Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu
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- <223> Synthetic construct
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 20 25 30
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- Cys Phe Tyr Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val 50 55 60
- Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala 65 70 75 80
- Gly Asn Val Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn 85 90 95
- Ser Pro Glu Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr 100 105 110
- Ile Gln Ser Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu 115 120 125

Asp Glu Arg Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg 130 135 140

Asp Val Phe Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser 145 150 155 160

Ser Ser Ser Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu 165 170 175

Ile Asp Val Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val 180 185 190

Ile Pro Ser Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu
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Ala 225

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Val Tyr Thr Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys 35 40 45

Cys Phe Tyr Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val 50 60

Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala 65 70 75 80

Gly Asn Val Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn 85 90 95

Ser Pro Glu Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr 100 105 110

Ile Gln Ser Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu
115 120 125

Asp Glu Arg Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg 130 135 140

Asp Val Phe Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser 145 150 155 160

Ser Ser Ser Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu 165 170 175

Ile Asp Val Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val 180 185 190

Ile Pro Ser Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu 195 200 205

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Ser His Ala Gly 225

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<211> 225

<212> PRT

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<221> Amino acid sequence of tTF-GCNGRCG

<223> Synthetic construct

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20 25 30

Val Tyr Thr Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys 35 40 45

Cys Phe Tyr Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val
50 60

Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala 65 70 75 80

Gly Asn Val Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn 85 90 95

Ser Pro Glu Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr

100 105 110

Ile Gln Ser Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu
115 120 125

Asp Glu Arg Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg 130 135 140

Asp Val Phe Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser 145 150 155 160

Ser Ser Ser Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu 165 170 175

Ile Asp Val Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val 180 185 190

Ile Pro Ser Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu
195 200 205

Cys Met Gly Gln Glu Lys Gly Glu Phe Arg Gly Cys Asn Gly Arg Cys 210 215 220

Gly 225

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<211> 232

<212> PRT

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<223> Synthetic construct

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Thr Asn Phe Lys Thr Ile Leu Glu Trp Glu Pro Lys Pro Val Asn Gln
20 25 30

Val Tyr Thr Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys
35 40 45

Cys Phe Tyr Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val 50 60

Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala 65 70 75 80

Gly Asn Val Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn

90 95

Ser Pro Glu Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr 100 105 110

Ile Gln Ser Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu
115 120 125

Asp Glu Arg Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg 130 135 140

Asp Val Phe Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser 145 150 155 160

Ser Ser Ser Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu 165 170 175

Ile Asp Val Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val 180 185 190

Ile Pro Ser Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu
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Cys Met Gly Gln Glu Lys Gly Glu Phe Arg Gly Cys Asn Gly Arg Cys 210 220

Val Ser Gly Cys Ala Gly Arg Cys 225 230

<210> 8

<211> 228

<212> PRT

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<220>

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<223> Synthetic construct

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Thr Asn Phe Lys Thr Ile Leu Glu Trp Glu Pro Lys Pro Val Asn Gln 20 25 30

Val Tyr Thr Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys 35 40 45

Cys Phe Tyr Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val 50 55 60

Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala

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Asp	Glu 130	Arg	Thr	Leu	Val	Arg 135	Arg	Asn	Asn	Thr	Phe 140	Leu	Ser	Leu	Arg		
Asp 145	Val	Phe	Gly	Lys	Asp 150	Leu	Ile	Tyr	Thr	Leu 155	Tyr	Tyr	Trp	Lys	Ser 160		
Ser	Ser	Ser	Gly	Lys 165	Lys	Thr	Ala	Lys	Thr 170	Asn	Thr	Asn	Glu	Phe 175	Leu		
Ile	Asp	Val	Asp 180	Lys	Gly	Glu	Asn	Tyr 185	Cys	Phe	Ser	Val	Gln 190	Ala	Val		
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aagtcaggag attggaaaag caaatgcttt tacacaacag acacagagtg tgacctcacc 1											18	30					
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addastataa adaggaccaa ttotactaga gagcototat atgagaacta coorgaatta 30											۱۸						

acaccttacc tggagacaaa cctcggacag ccaacaattc agagttttga acaggtggga 360
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ctaagcctcc gggatgtttt tggcaaggac ttaatttata cactttatta ttggaaatct 480
tcaagttcag gaaagaaaac agccaaaaca aacactaatg agtttttgat tgatgtggat 540
aaaggagaaa actactgttt cagtgttcaa gcagtgattc cctcccgaac agttaaccgg 600
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<223> Synthetic construct

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aagtcaggag attggaaaag caaatgcttt tacacaacag acacagagtg tgacctcacc	180									
gacgagattg tgaaggatgt gaagcagacg tacttggcac gggtcttctc ctacccggca	240									
gggaatgtgg agagcaccgg ttctgctggg gagcctctgt atgagaactc cccagagttc	300									
acacettace tggagacaaa ceteggacag ecaacaatte agagttttga acaggtggga	360									
acaaaagtga atgtgaccgt agaagatgaa cggactttag tcagaaggaa caacactttc	420									
ctaagcctcc gggatgtttt tggcaaggac ttaatttata cactttatta ttggaaatct	480									
tcaagttcag gaaagaaaac agccaaaaca aacactaatg agtttttgat tgatgtggat	540									
aaaggagaaa actactgttt cagtgttcaa gcagtgattc cctcccgaac agttaaccgg	600									
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aagtcaggag attggaaaag caaatgcttt tacacaacag acacagagtg tgacctcacc	180									
gacgagattg tgaaggatgt gaagcagacg tacttggcac gggtcttctc ctacccggca	240									
gggaatgtgg agagcaccgg ttctgctggg gagcctctgt atgagaactc cccagagttc	300									
acacettace tggagacaaa eeteggacag eeaacaatte agagttttga acaggtggga	360									
acaaaagtga atgtgaccgt agaagatgaa cggactttag tcagaaggaa caacactttc	420									

ctaagcctcc gggatgtttt tggcaaggac ttaatttata cactttatta ttggaaatct 480

tcaagttcag gaaagaaaac agccaaaaca aacactaatg agttttgat tgatgtggat 540
aaaggagaaa actactgttt cagtgttcaa gcagtgattc cctcccgaac agttaaccgg 600
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- <223> Synthetic construct
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660

675

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<210> 15

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<212> DNA
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<220>
<221> 5' Oligonucleotide primer for the preparation of tTF-GALNGRSHAG
<223> Synthetic construct
<400> 28
catgccatgg gatcaggcac tacaaatact gtggcagcat ataat
                                                                     45
<210> 29
<211> 55
<212> DNA
<213> Artificial
<220>
<221> 3' Oligonucleotide primer for the preparation of tTF-GALNGRSHAG
<223> Synthetic construct
<400> 29
cgggatccta ttaaccagcg tgagatcttc catttaaagc acctctgaat tcccc
                                                                     55
<210> 30
<211> 45
<212> PRT
<213> Artificial
<220>
<221> Amino acid sequence of the affinity-tag
<223> Synthetic construct
<400> 30
His His His His His Ser Ser Gly Leu Val Pro Arg Gly Ser Gly
               5
Met Lys Glu Thr Ala Ala Ala Lys Phe Glu Arg Gln His Met Asp Ser
Pro Asp Leu Gly Thr Asp Asp Asp Lys Ala Met Gly
                           40
<210> 31
<211> 269
<212> PRT
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<213> Artificial

<220>

<221> Amino acid squence of tTF-GRGDSP having an N-terminal affinity-tag <223> Synthetic construct

<400> 31

His His His His His Ser Ser Gly Leu Val Pro Arg Gly Ser Gly $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Met Lys Glu Thr Ala Ala Ala Lys Phe Glu Arg Gln His Met Asp Ser 20 25 30

Pro Asp Leu Gly Thr Asp Asp Asp Lys Ala Met Gly Ser Gly Thr 35 40 45

Thr Asn Thr Val Ala Ala Tyr Asn Leu Thr Trp Lys Ser Thr Asn Phe 50 55 60

Lys Thr Ile Leu Glu Trp Glu Pro Lys Pro Val Asn Gln Val Tyr Thr 65 70 75 80

Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys Cys Phe Tyr 85 90 95

Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val Lys Asp Val
100 105 110

Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala Gly Asn Val 115 120 125

Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn Ser Pro Glu 130 135 140

Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr Ile Gln Ser 145 150 155 160

Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu Asp Glu Arg 165 170 175

Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg Asp Val Phe 180 185 190

Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser Ser Ser Ser 195 200 205

Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu Ile Asp Val 210 215 220

Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val Ile Pro Ser 225 230 235 240

Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu Cys Met Gly 245 250 255

Gln Glu Lys Gly Glu Phe Arg Gly Arg Gly Asp Ser Asp

260 265

<210> 32

<211> 270 <212> PRT

<213> Artificial

<220>

 $<\!221\!>$ Amino acid sequence of tTF-GNGRAHA having an N-terminal affinity-tag $<\!223\!>$ Synthetic construct

<400> 32

His His His His His Ser Ser Gly Leu Val Pro Arg Gly Ser Gly $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15$

Met Lys Glu Thr Ala Ala Ala Lys Phe Glu Arg Gln His Met Asp Ser 20 25 30

Pro Asp Leu Gly Thr Asp Asp Asp Lys Ala Met Gly Ser Gly Thr 35 40 45

Thr Asn Thr Val Ala Ala Tyr Asn Leu Thr Trp Lys Ser Thr Asn Phe 50 55 60

Lys Thr Ile Leu Glu Trp Glu Pro Lys Pro Val Asn Gln Val Tyr Thr 70 75 80

Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys Cys Phe Tyr 85 90 95

Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val Lys Asp Val 100 105 110

Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala Gly Asn Val 115 120 125

Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn Ser Pro Glu 130 135 140

Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr Ile Gln Ser 145 150 155 160

Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu Asp Glu Arg 165 170 175

Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg Asp Val Phe
180 185 190

Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser Ser Ser Ser 195 200 205

Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu Ile Asp Val 210 215 220

Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val Ile Pro Ser

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225 230 235 240
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Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu Cys Met Gly 245 250 255

Gln Glu Lys Gly Glu Phe Arg Gly Asn Gly Arg Ala His Ala 260 265 270

<210> 33

<211> 6

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<400> 33

Gly Arg Gly Asp Ser Pro 1 5

<210> 34

<211> 7

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<400> 34

Gly Asn Gly Arg Ala His Ala

<210> 35

<211> 10

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<400> 35

Gly Ala Leu Asn Gly Arg Ser His Ala Gly $1 \hspace{1cm} 5 \hspace{1cm} 10$

<210> 36

<211> 7

<212> PRT

<213> Artificial

<220>

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<223> Synthetic construct
<400> 36
Gly Cys Asn Gly Arg Cys Gly
<210> 37
<211> 14
<212> PRT
<213> Artificial
<220>
<221> Cyclic
<223> Synthetic construct
<400> 37
Gly Cys Asn Gly Arg Cys Val Ser Gly Cys Ala Gly Arg Cys
                                    10
<210> 38
<211> 10
<212> PRT
<213> Artificial
<220>
<221> Cyclic
<223> Synthetic construct
<400> 38
Gly Cys Val Leu Asn Gly Arg Met Glu Cys
                                    10
<210> 39
<211> 10
<212> PRT
<213> Artificial
<220>
<223> Synthetic Construct
<400> 39
Thr Ala Ala Ser Gly Val Arg Ser Met His
                5
<210> 40
<211> 10
<212> PRT
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<213> Artificial

<220>
<223> Synthetic Construct

<400> 40

Leu Thr Leu Arg Trp Val Gly Leu Met Ser 1 5 10

<210> 41
<211> 8
<212> PRT
<213> Artificial

<220>
<223> Synthetic construct
<400> 41

Thr Thr His Trp Gly Phe Thr Leu 1 5
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